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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/557,796	04/25/2000	James Hoch	252/123	8950

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EXAMINER
LACOURCIERE, KAREN A

ART UNIT	PAPER NUMBER
1635	24

DATE MAILED: 07/14/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/557,796	HOCH ET AL.	
	Examiner	Art Unit	
	Karen A. Lacourciere	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 April 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *99-105,107-109 and 130-136* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *99-105,107-109 and 131-136* is/are rejected.

7)☒ Claim(s) *130* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 99-105, 107-109 and 130-136 are pending in the instant case.

Claim Rejections - 35 USC § 112

The rejections of record of claims 99-109 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn in response to Applicant's amendments filed April 16, 2003.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 99-104 and 107-109 are maintained as rejected and claims 131-134 are rejected under 35 U.S.C. 102(b) as being anticipated by Anderson et al. (US Patent No. 5,032,514).

Anderson et al. disclose recombinant bacterial cells comprising plasmids that comprise nucleic acids that encode polypeptides responsible for converting a source compound (for example, D-glucose) into a target compound (for example,

2-keto-D-gluconic acid) and further comprise genes responsible for converting the target compound into a detectable signal, including growth (for example, converting 2-keto-D-gluconic acid into 2,5-DKG, which is required for growth on minimal media plates) and wherein the nucleic acids comprising these genes comprise an inducible promoter. Anderson et al. further disclose recombinant cells wherein the target compound is 2-keto-gulonate. These target compounds are capable of being metabolized to carbon. Anderson et al. disclose their bacteria wherein the genes encoding the polypeptide that provide the detectable signal comprise and are under control of an inducible promoter, including the trp-lac hybrid promoter TacII. Therefore, Anderson et al. anticipates claims 99-104, 106-109 and 131-134.

Claims 99, 102, 104 and 105 are maintained as rejected under 35 U.S.C. 102(b) as being anticipated by Wood et al. (Applied and Environmental Microbiology, July 1992, Vol. 58, No. 7, p 2103-2110).

Wood et al. disclose recombinant Klebsiella oxytoca cells, wherein the cells comprise nucleic acids from Zymomonas mobilis that are responsible for converting a source compound (for example, amorphous cellulose) to a target compound which can be metabolized to carbon (for example, cellobiose). The cells disclosed by Wood et al. further comprise ncuelic acids in the geneome that express polypeptides that produce a detectable signal (for example growth) even in the presence of these compounds. The genome of K. oxytoca further

comprises genes under control of inducible promoters. Therefore, Wood et al. anticipates claims 99, 102, 104 and 105.

Response to arguments

Applicant's arguments filed April 16, 2003 have been fully considered but they are not persuasive.

In response to the rejection of record of claims 99-104 and 106-109 under 35 USC 102(b) as anticipated by Anderson et al. Applicant argues that the claimed invention is distinguished from Anderson et al. because the claims recite two distinct nucleic acid molecules. Applicant argues that in contrast Anderson et al. teaches bacterial cells comprising only one recombinant construct and then evaluates the endogenous metabolic pathways already present in the cell and does not teach the introduction of two distinct molecules into the cell. The rejected claims are directed to compositions, not methods, and, therefore, there is no step that requires introduction of two distinct nucleic acids into the cell.

These arguments are not found to be persuasive because Applicant is arguing limitations not found in the claims. The claimed cells do not require that the second nucleic acid be introduced into the cell, or be recombinant. As claimed, the first nucleic acid is recombinant, however, the second nucleic acid only needs to encode polypeptides that provide a detectable signal and comprise an inducible promoter, which reads on endogenous genes, including the metabolic pathways disclosed by Anderson et al.

In response to the rejection of record of claims 99, 102, 104 and 105 under 35 USC 102(b) as anticipated by Wood et al. Applicant argues that Wood et al. does not teach all of the limitations of the claimed cells because Wood et al. does not teach a recombinant nucleic acid molecule comprising an inducible promoter to control expression of the proteins encoded therein and further does not teach a nucleic acid molecule of any kind containing an inducible promoter.

These arguments have not been found to be persuasive because Applicant is arguing limitations that are not in the claims. The claims do not require a recombinant nucleic acid molecule comprising an inducible promoter, but rather any nucleic acid molecule comprising an inducible promoter and also comprising nucleic acids encoding proteins that provide a detectable signal. This reads even on a genomic DNA, as the second nucleic acid is not limited to recombinant DNA and genomic DNA comprises inducible promoters that control expression of proteins encoded by the genomic DNA. Therefore, the claims encompass the bacterial cells disclosed by Wood et al.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 135 and 136 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 135 is indefinite due to the recitation "Yia-operon related polypeptides". It is unclear what the metes and bounds of this term are, for example, what differences and what degree of difference can occur in a polypeptide such that it is considered to be related to a Yia-operon polypeptide versus an unrelated polypeptide. Claim 136 is indefinite for the same reasons due to dependence on claim 135.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 135 and 136 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 135 and 136 are drawn to cells comprising nucleic acids encoding Yia-operon related polypeptides including Yia J, YiaK, YiaL, ORF1, YiaX2, LyxK, YiaQ, YiaR and YiaS.

The specification discloses SEQ ID NO: 1 and 19 which corresponds to the genomic DNA encoding the klebsiella oxytoca species of yiaJ (SEQ ID NO:1) and the full klebsiella oxytoca yia operon (SEQ ID NO: 19, which comprises SEQ ID NO:1 and encodes K. oxytoca Yia J, YiaK, YiaL, ORF1, YiaX2, LyxK, YiaQ, YiaR and YiaS) and further discloses the sequence of the E. coli Yia operon nucleic acid was known in the prior art. SEQ ID NO: 1 and 19 and the E. coli operon meet the written description provisions of 35 USC 112, first paragraph. However, claims 135 and 136 are directed to encompass cells comprising nucleic acids encoding proteins from other species. None of these sequences meet the written description provision of 35 USC 112, first paragraph. Claims 135 and 136 are drawn to a broad genus of sequences (nucleic acids encoding Yia operon related polypeptides including Yia J, YiaK, YiaL, ORF1, YiaX2, LyxK, YiaQ, YiaR and YiaS), but the specification discloses only two species of this very broad genus. These species would not be representative of the claimed genus, such that one skilled in the art would recognize that the Applicant was in possession of the claimed genus. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of cells comprising SEQ ID NO: 1, 19 and the E. coli Yia-operon, the skilled artisan cannot envision the detailed chemical structure of

the polynucleotides encompassed in the claimed cells, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a

precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel* , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. No sequence information indicating which nucleotides constitute human cDNA appears in the patent, as appears for rat cDNA in Example 5 of the patent. Accordingly, the specification does not provide a written description of the invention of claim 5.

Therefore, only cells comprising SEQ ID NO: 1, 19 and the E. coli Yia operon, but not the full breadth of the claim, meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is

reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 99-102, 107, and 134-136 are rejected under 35 U.S.C. 102(b) as being anticipated by Badia et al. (JBC, Vol. 273, No. 14, p 8376-8381, cited in prior actions).

Badia et al. disclose bacterial cells wherein the cells comprise a first recombinant nucleic acid encoding polypeptides that convert source compounds to a target compound (e.g. the genomic DNA, which is recombinant, se for example, cell line description) and further comprises a nucleic acid encoding E. coli Yia-operon related polypeptides under control of an inducible promoter, wherein these Yia operon related polypeptides provide a detectable signal, including growth. Therefore, Badia et al. anticipates claims 99-102, 107, and 134-136.

Claim Objections

Claim 130 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Lacourciere whose telephone number is (703) 308-7523. The examiner can normally be reached on Monday-Thursday 8:30-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Karen A. Lacourciere
June 28, 2003

KAREN LACOURCIERE
PATENT EXAMINER